UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/142,597	03/05/99	COWDEN	W 120081.403

EXAMINER	
REVIS	

ART UNIT	PAPER NUMBER
1645	16

DATE MAILED: 03/21/01

000500 HM12/0321
SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 6300
SEATTLE WA 98104-7092

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/142,597	Applicant(s) Cowden et al.
	Examiner S. Devi, Ph.D.	Group Art Unit 1645

☒ Responsive to communication(s) filed on *12/27/2000.*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-4, 6-8, 15-17, and 19-21* ~~is/~~are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☒ Claim(s) *5, 9-14, 18, and 22-28* ~~is/~~are [redacted] canceled.

☒ Claim(s) *1-4, 6-8, 15-17, and 19-21* ~~is/~~are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Change of Art Unit Location

1) Effective 20 June 2000, the Art Unit location of your application in the US PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Technology Center 1600, Group 1640, Art Unit 1645.

Applicants' Amendment

2) Acknowledgment is made of Applicants' amendment filed 12/27/00 (paper no. 9) in response to the non-final Office Action mailed 06/21/00 (paper no. 7). With this, Applicants have amended the specification.

Status of Claims

3) Claims 5, 9-14, 18 and 22-28 have been canceled via the amendment filed 12/27/00.

Claims 1, 3 and 15 have been amended via the amendment filed 12/27/00.

Claims 1-4, 6-8, 15-17 and 19-21 are pending and are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

6) The objection to the specification made in paragraph 6 of the Office Action mailed 06/21/00 with regard to the format is withdrawn in light of Applicants' amendments to the specification.

7) The objection to claims 1 and 15 made in paragraph 5 of the Office Action mailed 06/21/00 is withdrawn in light of Applicants' amendments to the claims.

Rejection(s) Moot

8) The rejection of claims 5 and 18 made in paragraph 7 of the Office Action mailed 06/21/00

(paper no. 7) under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is moot in light of Applicants' cancellation of the claims.

9) The rejection of claims 5 and 18 made in paragraph 9 of the Office Action mailed 06/21/00 (paper no. 7) under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claims.

10) The rejection of claims 5 and 18 made in paragraph 11 of the Office Action mailed 06/21/00 (paper no. 7) under 35 U.S.C § 103(a) as being unpatentable over Qin *et al.* (*J. Immunol.* 150: 2072-2080, 1993) in view of Vodkin *et al.* (*J. Bacteriol.* 170: 1227-1234, 1988), Edgington (*Biotechnology* 13: 1442-1444, 13 December 1995) and Barnes *et al.* (WO 87/06590), is moot in light of Applicants' cancellation of the claims.

Rejection(s) Withdrawn

11) The rejection of claims 1-4, 6-8, 15-17 and 19-21 made in paragraph 9 of the Office Action mailed 06/21/00 (paper no. 7) under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendments to the claims and/or base claim(s).

Rejection(s) Maintained

12) The rejection of claims 1-4, 6-8, 15-17 and 19-21 made in paragraph 7 of the Office Action mailed 06/21/00 (paper no. 7) under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is maintained for reasons set forth therein and herebelow.

Applicants state that they have "amended the presently pending independent claims to the particular species, *C. burnetii* and to one or more antigenic components therefrom" (see page 3 of Applicants' amendment filed 12/27/00). Applicants contend that the specification at page 6 starting at lines 12 and 20, provides examples of a heat-killed or formalin-killed preparation of *C. burnetii* and a lysed preparation of the whole organism, a membrane/wall preparation, an endospore preparation and one or more purified or partially purified antigenic molecules therefrom. With regard to the treatment of any autoimmune disease, Applicants contend that no undue experimentation is required, because the specification provides sufficient guidance to allow one of ordinary skill in the art to identify antigenic components to verify the activity. Applicants further contend that an assertion of utility and/or enablement within a disclosure is presumed to be correct and that Applicants are not required to provide further evidence of the asserted utility or

enablement. Applicants state that the Office bears the initial burden of providing evidence showing that a person of ordinary skill in the art would reasonably doubt the disclosure.

Applicants' arguments have been carefully considered, but are found to be non-persuasive. First, contrary to the Applicants' statement, Applicants have **not** amended, i.e., limited, the pending independent claims to "*C. burnetii* and to one or more antigenic components therefrom" and a method of use of the same. Independent claims, currently under examination, still encompass any species of *Coxiella* and one or more antigenic components therefrom. As explained in paragraph 7 of the Office Action mailed 06/21/00, the scope of the claims currently encompasses "any" species of *Coxiella* and any forms of a *Coxiella* species, including, live (i.e., infective) *Coxiella* species for "use in preventing, inhibiting, delaying onset of or ameliorating the effects of autoimmune disease" in any mammal. Administration of a live, pathogenic *Coxiella* species would most likely infect a mammalian host rather than prevent, inhibit, delay onset of or ameliorate an autoimmune disease. Secondly, no evidence is of record within the instant specification that a membrane/wall preparation, an endospore preparation and one or more purified or partially purified (currently unidentified) antigenic molecules therefrom, "prevent, inhibit, delay onset of or ameliorate" the effects of "any" autoimmune disease. The applied art (see below) establishes that some antigens of *C. burnetii* are successfully used to treat autoimmune coxiellosis. However, with regard to the treatment of any non-coxiella-related autoimmune diseases, the specification does not teach how to identify the precise antigenic components that allegedly "prevent, inhibit, delay onset of or ameliorate" the effects of a broadly recited autoimmune disease, or provide any specific teachings of how to reproducibly produce these antigenic autoimmune-ameliorating antigenic components. This is critical in light of the art-recognized unpredictability of successfully treating an autoimmune disease with any component of a microbial antigen or any part of an already identified microbial antigen. For instance, one of the antigenic components recited in the instant specification for use in the claimed method of preventing, inhibiting, ameliorating or delaying the onset of an autoimmune disease in a mammal is an antigenic component that is analogous or homologous to that of a *Coxiella* sp. (see page 6, lines 6-10). It has been established in the art that an immunogenic hsp (heat shock protein) polypeptide of a mycobacterial species, such as *M. tuberculosis*, is analogous or homologous to

the heat shock protein (HSP) antigen of *Coxiella burnetii*. See abstract and the third full paragraph in the left column on page 1230 of Vodkin *et al.* (*J. Bacteriol.* 170: 1227-1234, 1988, already of record). The art also establishes that the mycobacterial 65-kDa heat-shock protein, which is analogous to the hsp of *Coxiella burnetii*, causes autoimmune arthritis (see Van Eden *et al. Rheumatol. Int.* 9: 187-191, 1989). The successful treatment of an autoimmune disease with such an antigenic component that is homologous or analogous to an antigenic component of a species of *Coxiella,* such as, *Coxiella burnetii*, is not predictable, because the highly conserved prokaryotic hsp molecules show as much as 50% homology or analogy in their amino acid sequence to that of human hsp, a self antigen (see Lamb *et al. Mol. Biol. Med.* 7: 311-321, 1990, see entire document, especially page 311). Because of this antigenic or molecular mimicry, hsp molecules cause autoimmune diseases including arthritis (see Jindal *et al. Mol. Cell Biol.* 9: 2279-2283, 1989; and Van Eden *et al. Nature* 331: 171-173, 1988). Therefore, induction of antibodies to such a whole antigenic component is unlikely to be therapeutic against any autoimmune disease.

Another example given on page 6 of the specification for an antigenic component of a *Coxiella* sp. for use in the claimed method is a membrane/wall preparation. The specification does not have evidentiary support showing that such a membrane/wall preparation of a *Coxiella* sp. does prevent, inhibit, ameliorate or delay onset of any non-coxiella-induced autoimmune disease, including IDDM. The art has established that several microbial cell wall components cause autoimmune conditions, such as, polyarthritis in a mammal rather than prevent, inhibit or ameliorate polyarthritis. See Van den Broek, *APMIS* 97: 861, 1989. Thus, there is no certainty that any *Coxiella* species, including live *Coxiella* species or any antigenic component of any species of *Coxiella*, would prevent, inhibit, ameliorate or delay onset of any non-coxiella-induced autoimmune disease, including IDDM. Therefore, other than QFA or QVAX of *C. burnetii*, which appear to be capable of treating the autoimmune effects of IDDM, instant specification is non enabling for any other *Coxiella* species or any other antigenic component of a *Coxiella* species (including *C. burnetii)* having such a therapeutic or prophylactic use against any autoimmune disease. Without specific identification and disclosure of specific anti-autoimmune antigenic components of a *Coxiella sp.* and without a demonstration of, or specific guidance as to

the use of such antigenic components for preventing, inhibiting, delaying onset of, or ameliorating the effects of sufficiently representative numbers of non-*Coxiella*-induced autoimmune diseases, including IDDM, one of ordinary skill in the art would not be able to make and use a therapeutic composition for the recited method or purpose and therefore, would not be able to reproducibly practice the claimed invention, without undue experimentation. Given the lack of guidance in the specification, the art-recognized unpredictability of successfully treating, inhibiting, preventing, delaying onset of, or ameliorating the effects of any autoimmune diseases, or IDDM in particular, with any *Coxiella* antigenic components, quantity of experimentation necessary and breadth of instant claims, one of ordinary skill in the art could not make or reproducibly practice the full scope of the instant invention, as claimed, without undue experimentation. The claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C § 112, first paragraph.

13) The rejection of claims 1, 2, 15, 16, 20 and 21 made in paragraph 12 of the Office Action mailed 06/21/00 (paper no. 7) under 35 U.S.C § 103(a) [not under 102(b) as incorrectly typed in the previous action] as being unpatentable over Zhang *et al.* (*Acta Virologica* 38: 327-332, 1994), or Gajdosova *et al.* (*Acta Virologica* 38: 339-344, 1994), each in view of Levy *et al.* (*Eur. J. Epidemiol.* 5: 447-453, 1989, abstract), or Roue *et al.* (*Lancet* 341: 1094-1095, 1993), is maintained for reasons set forth therein and herebelow.

Applicants contend that Zhang *et al.* or Gajdosova *et al.* do not teach a composition for preventing, inhibiting, delaying onset of or ameliorating the effects of an autoimmune disease in a mammal including IDDM. Applicants allege that the Office is indulging in "hindsight reconstruction" of the teaching of Levy *et al.* and Roue *et al.* Applicants state that even with the combination, the prior art does not even allude to the use of *C. burnetii* or an extract thereof to treat IDDM.

Applicants' arguments have been carefully considered, but are found to be non-persuasive. First, only claims 1, 2, 15, 16, 20 and 21 were rejected, but not "claims 1 to 15" as incorrectly stated by Applicants. Secondly, Applicants are correct in noting that the applied prior art references do not teach the use of *C. burnetii* to treat IDDM. That is why claims 3 and 5-8 were not rejected using the applied prior art. With regard to Applicants' statement that the Office is indulging in "hindsight reconstruction" of the teaching of Levy *et al.* and Roue *et al.*, it must be

recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicants' disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

It is noted that Applicants have not advanced any substantive arguments with regard to the teachings of the applied prior art with regard to the treatment, prevention or amelioration of autoimmune coxiellosis or Q fever. As clearly explained in paragraph 12 of the Office Action mailed 06/21/00, Zhang *et al.* teach a composition comprising a purified antigenic outer membrane protein component of *Coxiella burnetii* and its potential use as a subunit vaccine against Q fever. The antigenic component is contained in an adjuvant or a pharmaceutically acceptable carrier, and on administration to mice and guinea pigs, elicits both B-cell and T-cell mediated immunity in mice and guinea pigs and confers protection against challenge with *Coxiella burnetii* (see abstract; page 328, left column; Table 2 and Figure 2). Zhang *et al.* also teach the use of a suspension of killed phase I whole cell vaccines of *Coxiella burnetii* (i.e., QFA) in humans and animals (see page 327, left column).

Similarly, Gajdosova *et al.* teach a composition comprising phase I *Coxiella burnetii* whole cells or Cb I (i.e., QFA) and/or outer membrane components of *Coxiella burnetii* contained in a pharmaceutically acceptable carrier. A method of administering the compositions to mice for induction of protective humoral and cellular immunity is taught (see abstract; 'Materials and Methods' and 'Discussion'). Mice immunized with Cb I and an ONPC, i.e., a phase I trichloracetic extract (i.e., an antigenic component of *C. burnetii*), conferred highest degree of protection or resistance against challenge with *Coxiella burnetii* (see abstract and page 343, left column, second full paragraph). Although Zhang *et al.* or Gajdosova *et al.* do not expressly teach their composition for preventing, inhibiting or ameliorating an autoimmune disease in a mammal, Levy *et al.* teach the association between Q fever and autoimmune disorder by providing serological evidence of existence or development of autoimmune antibodies (see abstract) and Roue *et al.* teach that acute Q fever is associated with autoimmune disorders and development of autoimmune serological markers (see entire document, especially last paragraph).

Given the art recognized association between Q fever or coxiellosis and autoimmune manifestations as taught by Levy *et al.* or Roue *et al.*, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use Gajdosova's or Zhang's therapeutic antigenic composition(s) and method for preventing or ameliorating autoimmune Q fever or coxiellosis to produce the composition and the method of the instant invention, with a reasonable expectation of success. Since certain manifestations of Q fever are viewed as autoimmune disorders as taught by Levy *et al.* or Roue *et al.*, it is implicit that Gajdosova's or Zhang's therapeutic antigenic compositions prevent or ameliorate autoimmune Q fever or coxiellosis.

Remarks

14) Claims 1-4, 6-8, 15-17 and 19-21 stand rejected.

15) **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242.

17) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached

on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SD
S. Devi, Ph.D.
Patent Examiner
March 2001